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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/814,371	03/22/2001	Graham McCreath	8117-14	4297

23973 7590 12/14/2004

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/814,371	MCCREATH ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,9 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,9 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Susan Hanley is now the examiner for this application. Her contact information appears at the end of this Office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1, 3, 5, 9 and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "high" in claims 1 and 5 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification discloses two examples regarding Aα-chain integrity but does not indicate if the disclosed values are the standard for "high Aα-chain integrity." The prior art reports a number of different values for "A-α-chain integrity" that result from a purification scheme. However, the is no agreement on what constitutes "high Aα-chain integrity."

The phrase "wherein the fibrinogen binds to the resin" is confusing because it is unclear if the fibrinogen cited in this phrase refers to the "part-purified fibrinogen" in part c) or the "fibrinogen from milk" in part a) of the claim.

Claim Rejections - 35 USC § 103

Claims 1, 3, 5, 9 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garner et al. (US 5,639,940) in view of Tripodi (WO 9213495),Vukovich et al. (1980) and Lord (US 6,037,457), in further view of Holm et al. (1985) and Jennissen et al. (DE 4240119).

Applicant argues that none of the reference teach or suggest obtaining a fibrinogen with high Aα-chain integrity by the claimed method or the advantages of fibrinogen having said integrity. Applicant further asserts that the combined references do not suggest that the ability of the method to purify fibrinogen to a high Aα-chain integrity would be a foreseeable result by one of ordinary skill in the art.

The disclosures by Garner et al., Tripodi, Vukovich et al. and Lord are recapped:

Garner et al. disclose the transgenic production of fibrinogen from human or non-human sources in the milk of various livestock (column 2, lines 9-15; column 4, lines 15-20 and lines 30-33). The fibrinogen is recovered from the milk using standard practices such as precipitation, filtration and protein chromatography (column 2, line 65, column 9, lines 23-25).

Garner et al. lack the claim limitations regarding precipitating fibrinogen from milk in the presence of one or more of lysine, a lysine analog, or ε-aminocaproic acid, the specific HIC chromatography, and the new limitation that the recovered fibrinogen has a high Aα-chain integrity.

Tripodi discloses precipitating fibrinogen from plasma with PEG in a buffer containing e-aminocaproic acid. The buffer system is said to be important because it prevents premature conversion of fibrinogen into fibrin (page 8, line 34 to page 9, line 21).

Vukovich et al. (1980) teach that fibrinogen can be highly purified using HIC with for example, butyl-Sepharose.

Lord teaches that recombinantly produced fibrinogen can be purified by various techniques known in the art including precipitation and HIC (column 6, lines 36-52).

Jennissen et al. disclose the purification of human fibrinogen by applying plasma to a hydrophobic interaction column comprising pentyl-Sepharose. The yield of the purification was 25-60%. The purified fibrinogen was molecularly uniform and fully active. The purified human fibrinogen was subjected to SDS gel electrophoresis to characterize the individual chains of the purified fibrinogen. The molecular weight of the human Aα-chain was 72 kDa (col. 5, lines 20-55).

Holm et al. disclose the purification and characterization from human plasma wherein fresh human blood was combined with citrate and precipitated wit β-alanine. The precipitate was solubilized and then fractionated step-wise with ammonium sulfate to give three fractions (p. 165, abstract). The high molecular weight fibrinogen contained intact Aα-chains and no observable chain remnants (p. 170, lines 5-7). Holm et al. disclose that the molecule weight of the intact Aα-chain of fibrinogen is 70 kDa (p. 171, line 6).

The previous Office actions established that the claimed invention of combining the purification techniques and using ε-aminocaproic acid to prevent degradation was obvious because each of the references is directed to purifying fibrinogen from fluids such as milk. Hence, there is reasonable motivation to combine the references that have the same purpose. One of ordinary skill in the art would know that precipitation, separation, and HIC are all suitable methods of purifying fibrinogen based on the teachings of the Garner et al. A skilled artisan would look to the relevant fibrinogen purification art to find out further details of the process, including using ε-aminocaproic acid in the precipitation step.

Responding to Applicant's arguments, the ordinary artisan would have reasonably expected to obtain fibrinogen having high Aα-chain integrity when purifying fibrinogen by a combination of precipitation with ε -aminocaproic acid and HIC chromatography. Both Holm et al. and Jennissen et al. established that fibrinogen having high Aα-chain integrity can be obtained by employing precipitation or HIC chromatography *independently of one another*. Using only a precipitation step, Holm obtained fibrinogen with an intact Aα-chain integrity. Using only HIC chromatography, Jennissen et al. isolated fibrinogen having an Aα-chain with a molecular weight of 72 kDa. Based on the molecular weight taught by Holm et al., this value is within experimental error and the chain is intact. As previously stated in the rejection under 35 U.S.C. 112, the term "high" is undefined. However, one of ordinary skill in the art would judge an intact chain to have high integrity. Given that both methods independently yield fibrinogens with intact Aα-chains, the ordinary artisan would have reasonably foreseen that the combination of the methods to yield fibrinogen having high Aα-chain integrity.

In conclusion, it would have been obvious to the ordinary artisan to combine well known purification methods. Further, it would not have been surprising to the ordinary artisan to obtain fibrinogen having high Aα-chain integrity based on a privation procedure that combined the known methods. Therefore, the claims are prima facie obvious over the cited prior art.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

JEAN C. WITZ
PRIMARY EXAMINER

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
AU 1651